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| EXAMINER |
|---|
| ZHOU, SHUBO |

| ART UNIT | PAPER NUMBER |
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| 1631 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/767,701 | KOVALIC ET AL. | |
| | Examiner | Art Unit | |
| | SHUBO (Joe) ZHOU | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2 and 4-13* is/are pending in the application.

4a) Of the above claim(s) *10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/14/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Amendment/Response*

Applicant's amendment and request for reconsideration filed 5/14/08 are acknowledged and the amendment is entered.

Applicant's arguments filed 5/14/08 in response to the previous Office action mailed 2/14/08 have been fully considered but they are not deemed to be persuasive. The following rejections and/or objections are either reiterated from the previous Office action or newly added, necessitated by applicant's amendments, and constitute the complete set presently being applied to the instant application. Rejections and/or objections not reiterated from the previous Office action are hereby withdrawn.

### *Status of Claims*

Claims 2 and 4-13 are presently pending. Claims 10-13 have been previously withdrawn from further consideration for being drawing to nonelected invention, there being no allowable generic or linking claim. Therefore, only claims 2 and 4-9 are presently under consideration.

### *Claim Rejections-35 USC § 101/§ 112, First Paragraph*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 4-9 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The rejection is reiterated from the previous Office action mailed 2/14/08.

The amended claims are drawn to a recombinant polypeptide comprising an amino acid sequence of SEQ ID NO:44293, or a sequence that is at least 80%, 85%, 90% , 95%, 98%, or 99% identical with the amino acid sequence of SEQ ID NO:44293 or a fragment thereof. The claimed polypeptide is not supported by a specific and substantial asserted utility because none of the uses of the polypeptide as disclosed in the specification such as those detailed on pages 10-18, etc. is specific and substantial. For example, the specification states that the claimed recombinant polypeptide is involved in one or more important biological properties in a plant, that such recombinant polypeptide may be produced in transgenic plants to provide plants having improved phenotypic properties and/or improved response to stressful environmental conditions including cold tolerance, and that in some cases, decreased expression of such polypeptide may be desired (see at least page 10). These uses are not specific for the claimed polypeptide comprising a sequence of SEQ ID NO:44293. The specification generically lists a number of possible uses for the multitude polypeptides of SEQ ID NOS: 31565-63128, but fails to assert a specific utility for the claimed polypeptide comprising a sequence of SEQ ID NO:44293, and none of the utilities is specifically linked to the elected polypeptide. Recently, in *In re Fisher,* a case analogous to the present application, the court held that an asserted use must also show that the claimed invention can be used to provide a well-defined and particular benefit to the public and that "Fisher's claimed uses are nothing more than a 'laundry list' of research plans, each

general and speculative ... ." *In re Fisher*, 76 USPQ2d 1225 1229 1230 (CAFC 2005). In the instant application, the list of uses in the specification is akin to such a research plan and does not assert a particular and well-defined benefit to the public for the claimed polypeptide comprising an amino acid sequence of SEQ ID NO: 44293.

Furthermore, the claimed polypeptide is not supported by a substantial utility. For example, the specification states that the polypeptide can be used for improving stress tolerances, e.g. cold tolerance, in plants, etc. (page 11). However, this utility depends on the activity/function of the claimed polypeptide, and on the elucidation of the association of cold tolerance therewith, which are yet to be discovered through further research. The apparent need for such research indicates that the claimed polypeptide is not disclosed as to a currently available or substantial utility. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Also in *In re Fisher,* the court, following an analysis of Nelson, 626 F.2d at 856 with regard to substantial utility, states that "it thus is clear that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research." *In re Fisher*, 76 USPQ2d 1225 1230 (CAFC 2005). In the instant case, the application does not show that the claimed polypeptide is useful to the public as disclosed in its current form, but that it may prove useful at some future date after further research.

Additionally, neither the specification as filed nor any art of record discloses or suggests any property or activity for the polypeptide comprising an amino acid sequence of SEQ ID

NO:44293 such that another non-asserted utility would be well established for the claimed polypeptide.

While it is noted that the specification in Table 1 indicates that the polypeptide of SEQ ID NO:44293 shares sequence homology with the sequence of GENBANK accession number gi29150380, which appears to encode a synaptobrevin-like protein in *Oryza sativa*, one of skilled in the art would have reasonable doubt that the polypeptide of SEQ ID NO:44293 would indeed be a synaptobrevin-like protein for the following reasons:

Firstly, the sequence of gi29150380 is a sequence directly submitted to the GENBANK and the function of the sequence appears to be proposed only based on sequence comparisons with other sequences. See the enclosed printout of GENBANK accession No. AAO72389, which is also referred to as gi29150380.

Secondly, it would have been well known in the art that sequence similarity alone does not reliably correlate to identical or even similar biological activities. For example, it would have been well established in the art that even a single nucleotide or amino acid residue change or mutation in a sequence of a biomolecule would be sufficient to destroy the entire function of the biomolecule in many instances. Thus, in the absence of factual evidence characterizing the structural and functional aspects of the biomolecule, the effects of these changes would largely unpredictable as to which ones would have a significant effect and which ones would be silent mutations having no effect. The prior art cannot *unambiguously* assign function to an unknown gene or protein purely based on sequence homology comparisons. The following example demonstrates that assignment of a known function to a metabolic gene based on homology comparisons alone provides improper and erroneous functional assignment (see the homology-

based methods of functional assignment of Everett et al., Nature Genetics *17*, 411-422, **1997** in light of the experimental conclusions of Scott et al., Nature Genetics *21*, 440-443, **1999**). Everett et al. disclose a homology-based functional assignment to a putative, mutated sulfate transporter gene (PDS; which encodes "pendrin") identified through positional cloning in Pendred syndrome populations. The homology-based searches were carried out using BLAST and PSI-BLAST with commercial databases using the human pendrin clone as the query sequence. The conclusions of Everett et al. based upon the homology comparisons were that pendrin was a transporter of sulfate because it shared sequence homology with known sulfate transporter. The experimental studies by Scott et al., however, clearly demonstrate that pendrin, while having 29% homology to the rat sulfate-ion transporter encoded by *Sat-1*; 32% homology to the human diastrophic dysplasia sulfate transporter *DTD*; and 45% homology to the human sulfate transporter down-regulated in adenoma encoded by *DRA*, is actually not a transporter of sulfate, but rather that of chloride and iodine.

Thirdly, assuming *arguendo* that the polypeptide of SEQ ID NO: 44293 were indeed a synaptobrevin-like protein, one skilled in the art would have to perform further research to determine how much its activity/function is "like" synaptobrevin, and what specific and substantial utility a synaptobrevin-like protein might have in a plant. It had been known that there were different members of the synaptobrevin protein family. For instance, Raptis et al. (Journal of Chemical Neuroanatomy, Vol. 30, pages 201-211, 2005) disclosed that there were at least two isoforms of synaptobrevins: synaptobrevin/VAMP 1 and synaptobrevin/VAMP 2, which not only have different sequences, different distribution patterns, but also different specialized roles in the neurosecretory process in animals. See Abstract and page 202, left

column. Thus, it would require further research to at least determine (1) what exact function the polypeptide of SEQ ID NO:44293 would have, (2) would the protein be like synaptobrevin/VAMP 1 or synaptobrevin/VAMP 2, or both, (3) how much of its function would be "like" synaptobrevin, and (4) what specific and substantial utility a synaptobrevin-like protein might have in a plant . Once again, it is clear that the polypeptide of SEQ ID NO:44293 is not disclosed as to a currently available utility.

All the aforementioned references based upon in the above rejection have been provided to the applicant in the previous Office action mailed 4/24/06.

Applicant's arguments filed 5/14/08 have been fully considered but they are not found to be persuasive.

Applicant first argues that there are numerous utilities asserted in the specification regarding SEQ ID NO:44293 at page 19, line 12 through page 28, line 17 and in Table 1. See page 6 of the response. This is not found persuasive because at pages 19-28, the specification generically discusses recombinant DNA constructs, transformation methods and transgenic plants about thousands of polynucleotides including SEQ ID NOS 1-31564 encoding polypeptides of SEQ ID NOS: 31565-63128, but fails to assert a specific utility for the claimed polypeptide of SEQ ID NO:44293. As to Table 1, it only indicates that the polypeptide of SEQ ID NO:44293 shares sequence homology with the sequence of GENBANK accession number gi29150380, which appears to encode a synaptobrevin-like protein in *Oryza sativa*. However, as set forth above, one of skilled in the art would have reasonable doubt that the polypeptide of SEQ ID NO:44293 would indeed be a synaptobrevin-like protein for the aforementioned reasons.

Applicant further argues that the utility of SEQ ID NO:44293 is demonstrated by a BLASTP analysis and asserts that SEQ ID NO:44293 is 96% identical to a synaptobrevin 1 protein in Oryza sativa. Applicant provides that this alone is sufficient to satisfy the utility requirement under USC 101. See pages 6-7 of the response. This is not found persuasive because the mere fact that a sequence in question is homologous or even identical to a sequence known in a particular database does not necessarily indicate that there is a specific and substantial utility for the sequence in question if there is no known function and activity for the database sequence. In the instant case, the two sequences to which SEQ ID NO:44293 is homologous appear to have no known function in Oryza sativa. The database disclosure of CAD70274 seems to assert that the synaptobrevin-like protein "might involve in brassinolide signaling in rice." See the printout of CAD70274. However, the sequence was directly submitted to the database and there is no evidence supporting such assertion. Even today, there appears no experimental evidence indicating that synaptobrevin 1 is involved in brassinolide signaling in rice. Furthermore, given the sequences of CAD70274 and BAF21023 are not available to the public at the time of filing of the instant application, such utility – involving in brassinolide signaling -- would not have been readily apparent to one of skill in the art at the time the instant application was filed (1/29/2004). "Applicant cannot rebut the rejection by relying on a utility that would not have been readily apparent at the time the application was filed." See Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, January 5, 2001, page 1095, and *In re Wright* cited therein. Thus, even this utility that applicant asserted in the response is not deemed to be substantial. Lastly, given that there is no known, experimentally demonstrated activity/function for the synaptobrevin 1 in plant, one skilled in the art would have to perform further research to

determine a specific utility for the protein, and there is thus no substantial, readily available utility for the protein in plants.

Applicant further argues that the "specification discloses that nucleic acid sequences encoding the synaptobrevin-like protein can be introduced into a plant cell and transcribed using an appropriate promoter with such transcription resulting in the reduction or suppression of the endogenous synaptobrevin-like protein. Specification at page 19, line 12 through page 28, line 17. The modification of the expression can be monitored, for example, by using an ELISA assay, to raise specific antibodies to either a synaptobrevin 1 or synaptobrevin-like protein. Specification at page 25, line 16 through page 26, line 18. Such antibodies can be prepared using the claimed polypeptide sequences. Any one of these asserted utilities is specific, substantial and credible under the requirements of 35 U.S.C. § 101." See page 9 of the response. This is not found persuasive because a review of these sections of the specification reveals that the specification does not discloses as alleged by applicant as such. Thus, the specification does not even disclose one utility for the protein of SEQ ID NO:44293 that is specific and substantial.

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 4-9 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention lacks a patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established

utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The rejection is also reiterated from the previous Office action, and maintained for reasons set forth above.

Applicant's argument filed 5/14/08 has been fully considered and is not found to be persuasive for the same reasons as those set forth above.

***Claim Rejections-35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2 and 4-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Alexandrov et al. (EP 1033405 A2, September 6, 2000).

The reference and sequence alignments referred to in the following analysis have been provided to applicant in the Office action mailed 1/25/07.

This rejection was added in the previous Office action and it was necessitated by the amendments filed 11/26/07.

The claims are drawn to a recombinant polypeptide comprising an amino acid sequence of SEQ ID NO:44293 or a fragment thereof, or a sequence that is at least 80%, 85%, 90%, 95%,

98% or 99% identical with an amino acid sequence of SEQ ID NO:44293 or a fragment thereof. It is reasonably interpreted that the claim is drawn to a polypeptide comprising any fragment of SEQ ID NO:44293 that is two or more amino acid residues long.

Alexandrov et al. disclose multiple polypeptides including a polypeptide, a *Zea mays* polypeptide, comprising an amino acid sequence that shares a 99.5% overall match with the full-length sequence of the instant SEQ ID NO:44293. See the sequence alignment between SEQ ID NO:44293 and the sequence of database Geneseq accession number AAG44786, which is the same sequence as that of SEQ ID NO:56142 disclosed by Alenxandrov et al. The polypeptide disclosed by Alexandrov et al. comprises a sequence that is 100% (which is at least 80%, 85%, 90%, 95%, 98% or 99%) identical with a sequence of 107 amino acid residues long: from residue number 1 to residue number 107 of SEQ ID NO:44293. See the sequence alignment between SEQ ID NO:44293 and the sequence of database accession number AAG44786. See at least pages 327-328 for the production of recombinant proteins/polypeptides.

Applicant's arguments filed 5/14/08 have been fully considered but they are not found persuasive.

Applicant first disagrees with the examiner's assertion that the rejection was necessitated by applicant's amendment filed 11/26/07. Applicant argues that the Office previously cited the Alexandrov reference against the claims in the 1/25/07 final Office action and subsequently withdraw the rejections in the 9/6/07 Advisory. See page 12 of the response. This is not found persuasive because the reason the Alexandrov reference was used to reject the claims in the 1/25/07 Office action is that the claims contained the limitation that the claimed polypeptide comprises an amino acid sequence having at least 80% or 85% or 90% or 95% sequence identity

with "an amino acid sequence of SEQ ID NO:44293." As set forth in the 1/25/07 Office action, "an amino acid sequence of SEQ ID NO:44293 is construed as any fragment of SEQ ID NO:44293 including two or more amino acid residues long. See page 15 of the Office action. The reason why the rejection was withdrawn in the 9/6/07 Advisory action is that the limitation "an amino acid sequence of SEQ ID NO:44293" is amended to "the amino acid sequence of SEQ ID NO:44293," which is interpreted as the full-length sequence thereof. In the last Office action mailed 2/14/08, the reason why the Alesandrov reference is again used to reject the claims is that amendment filed 11/26/07 introduces the limitation of "or a fragment thereof" in the claims.

Applicant further argues that Alexandrov et al. is not prior art against the claims because the instant application claims priority at least to May 6, 1999. See page 12 of the response. This is not found persuasive. For the claimed SEQ ID NO:44293, applicant is not entitled to the filing dates of the prior applications as indicated in the Application Data Sheet filed 5/25/07 because the sequence is not found to be disclosed in any of the prior applications. Applicant is requested to indicate which particular SEQ ID NO(s) in those applications that is identical to the instant SEQ ID NO:44293 if applicant believes the instant application is entitled to the earlier filing dates.

## *Conclusion*

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Shubo Zhou/

Shubo (Joe) Zhou, Ph.D.

Primary Patent Examiner